

Kindly replace the paragraph beginning at page 21, line 13 with the following

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A Franz diffusion cell as disclosed above was used under conditions similar to those of example 1, unless otherwise noted. Permeation rate experiments were performed for 21 h. As a reference, the permeation rate from the saturated composition C in example 1 was determined to be 46 μ g per 21 h in a Franz diffusion cell experiment, as depicted in Figure 1. The experiments were all analysed by use of spectrophotometry. The results are depicted in Figure 2.

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Kindly delete the paragraph at page 24, lines 10-13 in its entirety.

Kindly replace the paragraph beginning at page 24, line 15 with the following:

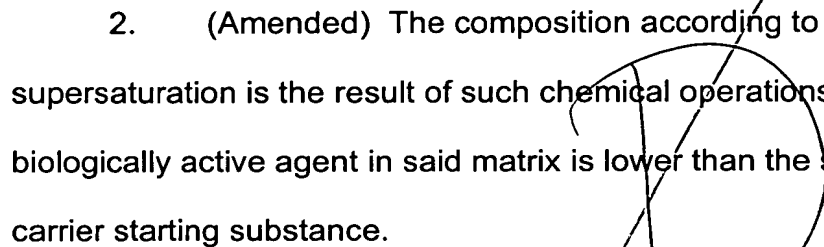
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Figure 2 shows that the chemical operation subjected to the compositions X1-X4 upon manufacturing of the compositions Y1-Y4 resulted in an increased thermodynamic potential of metronidazole, as is directly evidenced through the increased permeation rate. The permeation rate for a Y composition has increased approximately 40% in comparison with its corresponding X composition.

IN THE CLAIMS:

Please replace claims 1-29 as follows:

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1. (Amended) A biologically active composition comprising:
a biologically active agent to be released therefrom, wherein the biologically active composition is dissolved or dispersed in a carrier,

wherein said carrier is a liquid or solid non-crystalline matrix in which said biologically active agent is present in a supersaturated state, and wherein the supersaturated state is obtained by subjecting one or more carrier starting substances to chemical operations so that the liquid or solid non-crystalline increases until a supersaturated carrier matrix is provided, the biologically active agent being added before the chemical operations have been completed.


2. (Amended) The composition according to claim 1, wherein the supersaturation is the result of such chemical operations that the solubility of the biologically active agent in said matrix is lower than the solubility thereof in said carrier starting substance.

3. (Twice Amended) The composition according to claim 2, wherein said supersaturation is the result of chemical operations such that the degree of dissociation, aggregation or degree of protonation of the biologically active agent is different from the degree of dissociation, aggregation or degree of protonation of the agent in the carrier starting substance.

4. (Twice Amended) The composition according to claim 1, wherein the biologically active agent is added before the chemical operations have been initiated.

5. (Twice Amended) The composition according to claim 1, wherein the biologically active agent is added at a predetermined point of time after the chemical operations have been initiated, the composition thus obtained then being further subjected to the chemical operations.

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6. (Twice Amended) The composition according to claim 5, wherein the predetermined point of time is from 1 minute to 6 months after the chemical operations have been initiated.

7. (Amended) The composition according to claim 6, wherein the composition is further subjected to the chemical operations for a time period of about from 1 minute to 6 months.

8. (Twice Amended) The composition according to claim 1, wherein the starting substance, or said formed non-crystalline matrix, acts as a solvent or dispersing medium.

9. (Twice Amended) The composition according to claim 1, wherein the biologically active agent is added as a solid or liquid which is subsequently dissolved in the carrier.

10. (Twice Amended) The composition according to claim 1, wherein the biologically active agent is added in the form of a solution or dispersion.

11. (Twice Amended) The composition according to claim 1, wherein the biologically active agent is added above or around room temperature.

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cm 12. (Twice Amended) The composition according to claim 1, wherein the chemical operations comprise one or more chemical reactions.

13. (Amended) The composition according to claim 12, wherein the chemical reactions comprise etherifying, esterifying, hydrolysis, substitution, addition, elimination, oligomerising or polymerising reactions.

14. (Amended) The composition according to claim 13, wherein the chemical reactions are selected and performed so as to provide optimal delivery rate of the biologically active agent.

15. (Twice Amended) The composition according to claim 1, wherein the chemical operations involve subjecting the carrier starting substance to a temperature of from around -50°C to around 300°C.

16. (Twice Amended) The composition according to claim 1, wherein the chemical operations are conducted for a time period of from 1 minute to 6 months.

17. (Twice Amended) The composition according to claim 1, wherein the carrier starting substance, or mixture of two or more difference carrier starting

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cont

substances, is selected from the group consisting of monomers, acids, alcohols, ketones, aldehydes, amines, amides, anhydrides, lactides, glycolides, saccharides, acrylic or acrylamide compounds, monomers of PEO-diacrylate, cyanoacrylate, acrylate saccharides, acrylate lactate, acrylate glycolate, isocyanates, ethylene oxide, propylene oxide, pyrrolidone, PEO-diacrylate, ethylene-vinyl acetate, monomers of organic siloxanes, and oligomers, polymers and prepolymers thereof.

18. (Amended) The composition according to claim 17, wherein the acid is a monomeric acid and the alcohol is a monomeric alcohol, wherein the non-crystalline matrix comprises an ester or polyester thereof.

19. (Amended) The composition according to claim 18, wherein the monomeric acid is citric acid.

20. (Twice Amended) The composition according to claim 18, wherein the monomeric alcohol is propylene glycol.

21. (Twice Amended) The composition according to claim 1, which consists of one liquid or solid phase only.

22. (Twice Amended) The composition according to claim 1, wherein the biologically active agent is a pharmaceutically active agent.

23. (Twice Amended) The composition according to claim 22, wherein the pharmaceutically active agent is selected from the group consisting of guanosides, corticosteroids, psychopharmaceutical hormones, oxicams, peptides, proteins, antibiotics, antivirals, antimicrobials, anticancer agents, antifungals, oestrogens, antiinflammatory agents, neuroleptic agents, melanocyte stimulants and gland stimulants and agents with an effect on mast cell secretion.

24. (Amended) The composition according to any one of claims 22 and 23 for use as a medicament.

25. (Twice Amended) The composition according to claim 1, wherein the composition is applied topically to a mammal.

26. (Amended) A method for the preparation of a biologically active composition comprising:

dissolving or dispersing the biologically active composition in a carrier, and
subjecting a carrier starting substance, or a mixture of two or more different carrier starting substances, to chemical operations so that a liquid or solid non-crystalline carrier matrix is formed, in which the degree of saturation of said biologically active agent is increased until supersaturated, the biologically active agent is added before the chemical operations have been completed and in an amount such that a supersaturated state is obtained.

B1

27. (Twice Amended) The method according to claim 26, wherein the composition comprises a biologically active agent to be released therefrom, wherein the biologically active agent is dissolved or dispersed in a carrier, wherein the carrier is a liquid or solid non-crystalline matrix in which the biologically active agent is present in a supersaturated state, the supersaturated state being obtainable by subjecting one or more carrier starting substance to chemical operations so that the liquid or solid non-crystalline carrier matrix is provided in which the degree of saturation of the biologically active agent is increased until supersaturated, the biologically active agent being added before the chemical operations have been completed, and wherein the supersaturation is the result of chemical operations such that the solubility of the biologically active agent in the matrix is lower than the solubility thereof in carrier starting substance.

28. (Amended) The composition according to claim 2, wherein the supersaturation is the result of chemical operations such that the degree of dissociation, aggregation or degree of protonation of the biologically active agent is different from the degree of dissociation, aggregation or degree of protonation of the agent in the carrier starting substance.

29. (Amended) The composition according to claim 19, wherein the monomeric alcohol is propylene glycol.

Please add new claims 30-40 as follows:

30. (New) The composition of claim 17, wherein the acrylic or ^{acrylamide} acrylomide type compounds are methacrylate.

31. (New) The composition of claim 5, wherein said predetermined point of time is from 0.5 hours to 4 months after the chemical operations have been initiated.


32. (New) The composition of claim 31, wherein the composition is further subjected to the chemical operations for a time period from about 0.5 hours to 4 months.

33. (New) The composition of claim 23, wherein the melanocyte stimulants and gland stimulants are stimulators of sebaceous and pilo-sebaceous glands.

34. (New) The composition of claim 25, wherein the topical application is dermal.

35. (New) The composition of claim 25, wherein the mammal is man.

36. (New) The composition of claim 17, wherein acids are selected from the group consisting of mono-, di-, tri-acids and higher acids.

 37. (New) The composition of claim 17, wherein the alcohols are selected from the group consisting of mono-, di- and triols.

38. (New) The composition of claim 17, wherein the acrylate saccharides are acrylate starch.

39. (New) The composition of claim 1, wherein said chemical operations involve subjection the carrier substance to a temperature of from around 0°C to around 150°C.

40. (New) The composition of claim 1, wherein the chemical operations are conducted for a time period of from 0.5 hours to 4 months.
